We Claim:

1. A crosslinked protein crystal, said protein crystal being capable of change from insoluble and stable form to soluble and active form upon a change in the environment surrounding said crystal, said change being selected from the group consisting of: change in temperature, change in pH, change in chemical composition, change from concentrate to dilute form, change in shear force acting upon the crystal and combinations thereof.

2. The crosslinked protein crystal according to claim 1, wherein said change from concentrate to dilute form comprises a change in solute concentration.

3. The crosslinked protein crystal according to claim 2, wherein said change in solute concentration comprises an increase or decrease in salt concentration.

4. The crosslinked protein crystal according to claim 3, wherein said change in solute concentration comprises a decrease in salt concentration.

5. The crosslinked protein crystal according to claim 2, wherein said change in solute concentration comprises an increase or decrease in water concentration.

6. The crosslinked protein crystal according to claim 5, wherein said change in solute

concentration comprises an increase in water concentration.

7. The crosslinked protein crystal according to claim 2, wherein said change in solute concentration comprises an increase or decrease in organic solvent concentration.

8. The crosslinked protein crystal according to claim 2, wherein said change in solute concentration comprises a decrease in detergent concentration.

9. The crosslinked protein crystal according to claim 2, wherein said change in solute concentration comprises a decrease in protein concentration.

10. The crosslinked protein crystal according to claim 1, wherein said change from concentrate to dilute form comprises a change in concentration of all solutes from about 2-fold to about 10,000-fold.

11. The crosslinked protein crystal according to claim 10, wherein said change from concentrate to dilute form comprises a change in concentration of all solutes from about 2-fold to about 700-fold.

12. The crosslinked protein crystal according to claim 1, wherein said change in pH comprises a change from acidic pH to basic pH.

13. The crosslinked protein crystal according to claim 1, wherein said change in pH comprises a change from basic pH to acidic pH.

14. The crosslinked protein crystal according to claim 1, wherein said change in temperature comprises an increase or decrease in temperature.

15. The crosslinked protein crystal according to claim 14, wherein said change in temperature is an increase in temperature from a low temperature between about 0°C and about 20°C to a high temperature between about 25°C and about 70°C.

16. The crosslinked protein crystal according to claim 1, wherein said active form of said protein is a form which is active against macromolecular substrates.

17. A crosslinked protein crystal, said protein crystal having a half-life of activity under storage conditions which is greater than at least 2 times that of the soluble form of the protein that is crystallized to form said crystal that is crosslinked and activity similar to that of the soluble form of the protein under conditions of use.

18. A crosslinked protein crystal, said protein crystal being capable of releasing its protein activity at a controlled rate upon exposure to a change in the environment surrounding said crystal, said change being selected from the group consisting of change in pH, change in solute concentration, change in

temperature, change in chemical composition, change in shear force acting upon the crystals and combinations thereof.

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19. The crosslinked protein crystal according to claim 18, wherein said controlled rate of releasing protein activity is determined by a factor selected from the group consisting of: the degree of crosslinking of said crosslinked protein crystal, the length of time of exposure of protein crystal to the crosslinker, the rate of addition of the crosslinking agent to said protein crystal, the nature of the crosslinker, the chain length of the crosslinker, the surface area of said crosslinked protein crystal, the size of said crosslinked protein crystal, the shape of said crosslinked protein crystal and combinations thereof.

20. The crosslinked protein crystal according to claim 18, wherein said crystal has a protein activity release rate of between about 0.1% per day and about 100% per day.

21. The crosslinked protein crystal according to claim 18, wherein said crystal has a protein activity release rate between about 0.01% per hour and about 100% per hour.

22. The crosslinked protein crystal according to claim 18, wherein said crystal has a protein activity release rate between about 1% per minute and about 50% per minute.

23. The crosslinked protein crystal according to any one of claims 1, 17 or 18, said protein crystal being substantially insoluble and stable in a composition under storage conditions and substantially soluble and active under conditions of use of said composition.

24. The crosslinked protein crystal according to claim 23, wherein said composition is selected from the group consisting of cleaning agents, detergents, personal care compositions, cosmetics, pharmaceuticals, veterinary compounds, vaccines, foods, feeds, diagnostics and formulations for decontamination.

25. The crosslinked protein crystal according to claim 24, wherein said detergent is selected from the group consisting of powdered detergents, liquid detergents, bleaches, household cleaners, hard surface cleaners, industrial cleaners, carpet shampoos and upholstery shampoos.

26. The crosslinked protein crystal according to claim 24, wherein said cosmetic is selected from the group consisting of creams, emulsions, lotions, foams, washes, gels, compacts, mousses, sunscreens, slurries, powders, sprays, foams, pastes, ointments, salves, balms, shampoos, sunscreens and drops.

27. The crosslinked protein crystal according to any one of claims 1, 17 or 18, wherein said protein is an enzyme.

28. The crosslinked protein crystal according to claim 27, wherein said enzyme is selected from the group consisting of hydrolases, isomerases, lyases, ligases, transferases and oxidoreductases.

29. The crosslinked protein crystal according to claim 28, wherein said enzyme is selected from the group consisting of proteases, amylases, cellulases, lipases and oxidases.

30. The crosslinked protein crystal according to any one of claims 1, 17 or 18, wherein said protein is selected from the group consisting of therapeutic proteins, cleaning agent proteins, personal care proteins, veterinary proteins, food proteins, feed proteins, diagnostic proteins and decontamination proteins.

31. The crosslinked protein crystal according to any one of claims 1, 17 or 18, wherein said protein is selected from the group consisting of hormones, antibodies, inhibitors, growth factors, trophic factors, cytokines, lymphokines, toxoids, growth hormones, nerve growth hormones, bone morphogenic proteins, toxoids, vitamins and nutrients.

32. The crosslinked protein crystal according to any one of claims 1, 17 or 18, wherein said protein is selected from the group consisting of insulin, amylin, erythropoietin, Factor VIII, TPA, dornase-α, α-1-antitripsin, urease, fertility hormones, FSH, LSH, postridical hormones, tetanus toxoid and diptheria toxoid.

33. The crosslinked protein crystal according to any one of claims 1, 17 or 18, said crystal having a longest dimension of between about 0.01 µm and about 500 µm.

34. The crosslinked protein crystal according to any one of claims 1, 20 or 21, said crystal having a longest dimension of between about 0.1 µm and about 50 µm.

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35. The crosslinked protein crystal according to any one of claims 1, 17 or 18, said crystal having a shape selected from the group consisting of: spheres, needles, rods, plates, rhomboids, cubes, bipryamids and prisms.

36. A composition comprising a crosslinked protein crystal according to any one of claims 1, 17 or 18, said composition being selected from the group consisting of cleaning agents, detergents, personal care compositions, cosmetics, pharmaceuticals, veterinary compounds, vaccines, foods, feeds, diagnostics and formulations for decontamination.

37. The composition according to claim 36, wherein said detergent is selected from the group consisting of powdered detergents, liquid detergents, bleaches, household cleaners, hard surface cleaners, industrial cleaners, carpet shampoos and upholstery shampoos.

38. The composition according to claim 36, wherein said cosmetic is selected from the group consisting of creams, emulsions, lotions, foams,

washes, gels, compacts, sunscreens, slurries, powders, sprays, foams, pastes, ointments, salves, balms, shampoos, sunscreens and drops.

39. A protein delivery system, said system comprising crosslinked protein crystals according to any one of claims 1, 17 or 18.

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40. The protein delivery system according to claim 39, wherein said protein is selected from the group consisting of: detergent enzymes, cosmetic proteins, pharmaceutical proteins, agricultural proteins, vaccine proteins and decontamination proteins.

41. The protein delivery system according to claim 40, said protein delivery system being a microparticulate protein delivery system.

42. The protein delivery system according to claim 41, wherein said microparticulate protein delivery system comprises crosslinked protein crystals having a longest dimension between about 0.01 $\mu$m and about 500 $\mu$m.

43. The protein delivery system according to claim 42, wherein said microparticulate protein delivery system comprises crosslinked protein crystals having a longest dimension of between about 0.1 $\mu$m and about 50 $\mu$m.

44. The protein delivery system according to claim 41, wherein said microparticulate protein delivery system comprises crosslinked protein crystals

having a shape selected from the group consisting of: spheres, needles, rods, plates, rhomboids, cubes, bipryamids and prisms.

45. A detergent formulation comprising a crosslinked protein crystal according to any one of claims 1, 17 or 18.

46. A controlled release formulation comprising a crosslinked protein crystal according to any one of claims 1, 17 or 18.

47. A pharmaceutical controlled release formulation comprising a crosslinked protein crystal according to any one of claims 1, 17 or 18.

48. A pharmaceutical controlled release formulation comprising a crosslinked protein crystal, said crystal being substantially insoluble under storage conditions and capable of releasing its protein activity in vivo at a controlled rate.

49. The pharmaceutical controlled release formulation according to claim 47, said pharmaceutical being capable of administration by parenteral or non-parenteral routes.

50. The pharmaceutical controlled release formulation according to claim 49, said pharmaceutical being capable of administration by oral, pulmonary, nasal, aural, anal, dermal, ocular, intravenous, intramuscular, intraarterial, intraperitoneal, mucosal, sublingual, subcutaneous or intracranial route.

51. The pharmaceutical controlled release formulation according to claim 47, wherein said pharmaceutical is capable of administration by oral route and said crosslinked protein crystal is substantially insoluble under gastric pH conditions and substantially soluble under small intestine pH conditions.

52. A vaccine comprising a crosslinked protein crystal according to any one of claims 1, 17 or 18.

53. A formulation comprising a crosslinked protein crystal according to any one of claims 1, 17 or 18, said formulation being selected from the group consisting of tablets, liposomes, granules, spheres, microspheres, microparticles and capsules.

54. A method for producing crosslinked protein crystals comprising the step of reacting protein crystals with a first crosslinking agent, or a first crosslinking agent and at least a second crosslinking agent, under conditions sufficient to induce crosslinking of said crystals to the extent that the resulting crosslinked crystals are characterized by the ability to change from insoluble and stable form to soluble and active form upon a change in their environment, said change being selected from the group consisting of change in temperature, change in pH, change in chemical composition, change from concentrate to dilute form, change in shear force acting upon the crystals and combinations thereof.

55. A method for producing crosslinked protein crystals comprising the step of reacting protein crystals with a first crosslinking agent, or a first crosslinking agent and at least a second crosslinking agent, under conditions sufficient to induce crosslinking of said crystals to the extent that the resulting crosslinked crystals are characterized by a half-life of activity under storage conditions which is greater than at least 2 times that of the soluble form of the protein that is crystallized to form said crystals that are crosslinked and activity similar to that of the soluble form of the protein under conditions of use.

56. A method for producing crosslinked protein crystals comprising the step of reacting protein crystals with a first crosslinking agent, or a first crosslinking agent and at least a second crosslinking agent, under conditions sufficient to induce crosslinking of said crystals to the extent that the resulting crosslinked crystals are characterized by being capable of releasing their protein activity at a controlled rate upon exposure to a change in their environment, said change being selected from the group consisting of change in pH, change in soluble concentration, change in temperature, change in chemical composition, change in shear force acting upon the crystals and combinations thereof.

57. The method for producing crosslinked protein crystals according to any one of claims 54, 55 or 56, comprising the step of reacting said protein crystals with said first crosslinking agent and said at

least a second crosslinking agent at the same time or in sequence.

58. The method for producing crosslinked protein crystals according to any one of claims 54, 55 or 56, wherein, prior to reacting protein crystals with said crosslinking agent, said method further comprises the step of crystallizing said protein.

59. The method for producing crosslinked protein crystals according to any one of claims 54, 55 or 56, wherein the conditions sufficient to induce crosslinking are dependent upon a factor selected from the group consisting of: the degree of crosslinking of said crosslinked protein crystals, the length of time of exposure of protein crystals to the crosslinking agent, the rate of addition of the crosslinking agent to said protein crystal, the nature of the crosslinker, the chain length of the crosslinker, the surface area of said crosslinked protein crystals, the size of said crosslinked protein crystals, the shape of said crosslinked protein crystals and combinations thereof.

60. The method for producing crosslinked protein crystals according to claim 56, wherein said controlled rate of releasing protein activity is determined by a factor selected from the group consisting of: the degree of crosslinking of said crosslinked protein crystals, the length of time of exposure of protein crystals to the crosslinking agent, the rate of addition of the crosslinking agent to said protein crystals, the nature of the crosslinker, the chain length of the crosslinker, the surface area of said crosslinked protein crystals, the size of said

crosslinked protein crystals, the shape of said crosslinked protein crystals and combinations thereof.

61. The method for producing crosslinked protein crystals according to any one of claims 54, 55 or 56, wherein said crosslinking agent is a multifunctional crosslinking agent.

62. The method for producing crosslinked protein crystals according to claim 61, wherein said crosslinking agent is a bifunctional crosslinking agent.

63. The method for producing crosslinked protein crystals according to claim 61, wherein said crosslinking agent is selected from the group consisting of: glutaraldehyde, succinaldehyde, octanedialdehyde and glyoxal.

64. The method for producing crosslinked protein crystals according to claim 61, wherein said crosslinking agent is selected from the group consisting of: halo-triazines, halo-pyrimidines, anhydrides of aliphatic or aromatic mono- or di-carboxylic acids, halides of aliphatic or aromatic mono- or di-carboxylic acids, N-methylol compounds, di-isocyanates, di-isothiocyanates and aziridines.

65. The method for producing crosslinked protein crystals according to any one of claims 54, 55 or 56, wherein said crosslinking agent is an epoxide.

66. The method for producing crosslinked protein crystals according to claim 65, wherein said

epoxide is selected from the group consisting of: neopentyl glycol diglycidyl ether, ethylene glycol diglycidyl ether, di-epoxides, tri-epoxides and tetra-epoxides.

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67. The method for producing crosslinked protein crystals according to any one of claims 54, 55 or 56, wherein said crosslinking agent is 0.0076% to 0.5% glutaraldehyde and wherein the conditions sufficient to induce crosslinking include reacting protein crystals with a crosslinking agent for a period of time between about 3 minutes and about 120 minutes.

68. The method for producing crosslinked protein crystals according to claim 67, wherein said crosslinking agent is 0.005% glutaraldehyde and wherein the conditions sufficient to induce crosslinking include reacting protein crystals with a crosslinking agent for a period of time between about 10 minutes and about 30 minutes.

69. The method for producing crosslinked protein crystals according to claim 67 wherein, prior to reaction with said protein crystals, said glutaraldehyde is pretreated by incubation at 60°C with a buffer for 1 hour.

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70. The method for producing crosslinked protein crystals according to any one of claims 54, 55 or 56, wherein said crosslinking agent is 0.01% to 1% glyoxal and wherein the conditions sufficient to induce crosslinking include reacting protein crystals with a crosslinking agent for a period of time between about 30 minutes and about 60 minutes.

71. The method for producing crosslinked protein crystals according to any one of claims 54, 55 or 56, wherein said crosslinking agent is 0.05% to 1% octanedialdehyde and wherein the conditions sufficient to induce crosslinking include reacting protein crystals with a crosslinking agent for a period of time between about 30 minutes and about 16 hours.

72. The method for producing crosslinked protein crystals according to claim 71, wherein said crosslinking agent is 1% octanedialdehyde and wherein the conditions sufficient to induce crosslinking include reacting protein crystals with a crosslinking agent for a period of time between about 1 hour and about 3 hours.

73. The method for producing crosslinked protein crystals according to any one of claims 54, 55 or 56, wherein said crosslinking agent is 1% succinaldehyde and wherein the conditions sufficient to induce crosslinking include reacting protein crystals with a crosslinking agent for a period of time between about 30 minutes and about 3 hours.

74. The method for producing crosslinked protein crystals according to any one of claims 54, 55 or 56, wherein said first crosslinking agent is 0.01% to 4% epoxide and said second crosslinking agent is 0.1% to 0.2% glutaraldehyde and wherein the conditions sufficient to induce crosslinking include reacting said protein crystals with said first crosslinking agent for a period of time between about 1 hour and about 72 hours and reacting said protein crystals with said

second crosslinking agent for a period of time between about 1 hour and about 5 hours.

75. The method for producing crosslinked protein crystals according to claim 74, wherein said first crosslinking agent is 0.01% epoxide and said second crosslinking agent is 0.1% glutaraldehyde and wherein the conditions sufficient to induce crosslinking include reacting said protein crystals with said first crosslinking agent for about 5 hours and reacting said protein crystals with said second crosslinking agent for about 1.5 hours.

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76. The method for producing crosslinked protein crystals according to any one of claims 54, 55 or 56, wherein said protein is an enzyme.

77. The method for producing crosslinked protein crystals according to any one of claims 54, 55 or 56, wherein said crosslinking agent is a reversible crosslinking agent.

78. The method for producing crosslinked protein crystals according to claim 77, wherein said reversible crosslinking agent is a disulfide crosslinking agent.

79. The method for producing crosslinked protein crystals according to claim 78, wherein said disulfide crosslinking agent is a homobifunctional crosslinking agent or a heterobifunctional crosslinking agent.

80. The method for producing crosslinked protein crystals according to any one of claims 54, 55 or 56, wherein said protein is an enzyme.

81. The method for producing crosslinked protein crystals according to claim 80, wherein said enzyme is selected from the group consisting of hydrolases, isomerases, lyases, ligases, transferases and oxidoreductases.

82. The method for producing crosslinked protein crystals according to claim 81, wherein said enzyme is from the group consisting of proteases, amylases, cellulases, lipases and oxidases.

83. The method for producing crosslinked protein crystals according to any one of claims 54, 55 or 56, wherein said protein is selected from the group consisting of therapeutic proteins, cleaning agent proteins, personal care proteins, veterinary proteins, food proteins, feed proteins, diagnostic proteins and decontamination proteins.

84. The method for producing crosslinked protein crystals according to claim 83, wherein said protein is selected from the group consisting of hormones, antibodies, inhibitors, growth factors, trophic factors, cytokines, lymphokines, toxoids, growth hormones, nerve growth hormones, bone morphogenic proteins, toxoids, vitamins and nutrients.

85. The method for producing crosslinked protein crystals according to claim 84, wherein said protein is selected from the group consisting of

insulin, amylin, erythropoietin, Factor VIII, TPA, dornase-α, α-1-antitripsin, urease, fertility hormones, FSH, LSH, postridical hormones, tetanus toxoid and diptheria toxoid.

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